

REMARKS

Claims 3-5, 23, and 26-30 have been cancelled. Accordingly, the remarks below only address the Office's rejections to claims 1-2, 22, and 25, which are presently pending and stand rejected under 35 U.S.C. §103(a). The claim amendments and new claims are supported by the specification and do not contain new matter.¹

A hard copy of the sequence listing and a computer readable format is enclosed. The specification has been amended to include sequence identification numbers.

I. 35 U.S.C. 103(a) Rejection

Reconsideration is requested of the rejection of claims 1-2, 22, and 25 under 35 U.S.C. §103(a) in view of Senn-Bilfinger², Ruwart³, and Lindberg et al.⁴

Claim 1, as amended, is directed to a method of treating a **herpetoviridae** infection in a subject. The method involves administering to the subject a therapeutically effective amount of a sulfur-containing compound, where the compound is an **inhibitor of a (H⁺/K⁺) ATPase** and an **inhibitor of a herpetoviridae protease**.

Senn-Bilfinger disclose a class of substituted benzimidazoles that inhibit gastric acid secretions.⁵ Because the compounds inhibit gastric acid secretions, Senn-Bilfinger disclose that the compounds are effective in treating illnesses that are diseases of the stomach and intestine, such as gastric ulcers, duodenal ulcers, or gastritis resulting from gastric acid secretions.⁶

¹The addition of herpetoviridae to claim 1 is supported by the specification on page 5, at lines 25-30. The addition of alkyl thio and sulfone to claim 2 is supported by the specification on page 5, at lines 10-14. New claim 31 is supported by the specification on page 5, at lines 35-37. New claim 32 is supported by the specification on page 3, at lines 30-35 and on page 142, at Table 2.

² Senn-Bilfinger, U.S. Patent No. 4,472,409.

³Ruwart, U.S. Patent No. 4,359,465.

⁴Lindberg et al., (1987) TIPS 8:399-402.

⁵See Senn-Bilfinger, at column 1, lines 53-60.

⁶See Senn-Bilfinger, at column 11, lines 35-65; also see column 14 detailing the examples where the compounds ability to prevent gastric ulcers is attributed to their ability to inhibit gastric secretions.

Ruwart disclose the use of heterocyclalkylsulfanylbenzimidazoles for the treatment or prevention of **gastroint stinal inflammatory dis ases**, such as gastric ulcers, duodenal ulcers, and intestinal inflammatory disease.⁷ Moreover, according to Ruwart, the compounds are effective in preventing gastrointestinal inflammatory diseases at the dosages administered because of their **anti-inflammatory properties**.⁸

Senn-Bilfinger and Ruwart, either alone or in combination, do not disclose or suggest a method to treat **herpetoviridae infection** in a subject, as required by claim 1. Senn-Bilfinger and Ruwart also do not disclose or suggest sulfur-containing compounds that are dual inhibitors of **a (H⁺/K⁺) ATPase** and **a herpetoviridae protease**. Instead, the cited art discloses compounds that may be employed in methods to treat gastric ulcers, duodenal ulcers or gastritis resulting from either excessive gastric acid secretion, as disclosed in Senn-Bilfinger, or resulting from a gastro-inflammatory response, as disclosed in Ruwart.

Lindberg et al. disclose a class of gastric acid secretion inhibitors, omeprazole, which prevent gastric acid secretion by inhibiting the gastric H⁺/K⁺ ATPase.⁹ According to Lindberg et al., the primary use of the compounds is for the treatment of **gastric ulcers**.¹⁰ Lindberg et al. do not disclose or suggest a method to treat **herpetoviridae infection**. Lindberg et al. also do not disclose or suggest sulfur-containing compounds that are dual inhibitors of **a (H⁺/K⁺) ATPase** and **a herpetoviridae protease**, as required by claim 1.

In the absence of any disclosure of these elements of the method defined in claim 1, a *prima facie* case for obviousness is lacking.

According to the Office, the cited art renders claim 1 obvious because Senn-Bilfinger and Ruwart are said to teach that benzimidazoles have antiviral activity, and Lindberg is said to teach that benzimidazoles are inhibitors of (H⁺/K⁺) ATPase activity. Taken together, the Offices asserts that "one of ordinary skill would be motivated to use the benzimidazoles having inhibiting property of (H⁺/K⁺) ATPase activity of Lindberg et al, in the treatment of viral infection of Senn-Bilfinger and Ruwart, with the reasonable

⁷See Ruwart, at column 1, lines 5-10.

⁸See Ruwart, at column 8, lines 35-45 where it is disclosed administration of the compounds results in "total prevention of the inflammatory process."

⁹Lindberg et al. see abstract.

¹⁰*Id.*

expectation of treating viral infection, *absent evidence to the contrary*."¹¹ In fact, Applicants' application provides such "evidence to the contrary." As set-forth above, Lindberg et al. discloses that **omeprazole** is a (H⁺/K⁺) ATPase inhibitor. Table 2 in the present specification details results comparing the ability of a number compounds that are (H⁺/K⁺) ATPase inhibitors to inhibit assemblin (i.e., a serine viral protease). One of the compounds tested was omeprazole (i.e., the compound disclosed by Lindberg et al.) and it was found to have 0% assemblin inhibition activity.¹² If a skilled artisan had made the Office's proposed substitution, accordingly, they would not have arrived at the method of claim 1.

In addition, Ruwart and Senn-Bilfinger do not disclose or suggest that benzimidazoles have anti-herpetoviridae activity. Ruwart specifically states:

...these inflammatory diseases are known to be caused by a wide variety of agents present in the gastrointestinal tract which are known to attack the surfaces thereof, producing an inflammatory response. Such agents include microorganisms (viruses and fungi), bacterial toxins...¹³

Ruwart, contrary to the Office's assertion, merely states that viruses are one of several agents that may cause inflammatory diseases. Nowhere does Ruwart disclose or suggest use of any class of sulfur-containing compounds as anti-viral agents or as agents to treat **herpetoviridae infection**, as required by the method of claim 1. Additionally, Senn-Bilfinger specifically states "(British Pat. No. 1,234,058) concerns *benzazole derivatives* which are said to have a tuberculostatic, insecticidal, fungicidal, antiviral, anthelmintic and anti-inflammatory action..."¹⁴ Benzazoles, as disclosed in Senn-Bilfinger, typically contain carbon and nitrogen. While benzazole derivatives may contain sulfur or oxygen or other atoms, nowhere does Senn-Bilfinger indicate that the particular "benzazole derivatives" referred to as having "anti-viral activity" are sulfur-containing compounds, as required by the method of claim 1. Nowhere does Senn-Bilfinger disclose or suggest that "anti-viral" encompasses "anti-herpetoviridae," as required by the method of claim 1. The disclosure of Ruwart and Senn-Bilfinger regarding "anti-viral" and compounds that have "anti-viral" activity, would not lead a

¹¹See Paper 6 at page 4 (emphasis added).

¹²See page 142 of the specification.

¹³See Ruwart, at column 1, lines 45-50.

¹⁴See Senn-Bilfinger, at column 1, lines 15-20 (emphasis added).

skilled artisan to select sulfur-containing compounds that are dual inhibitors of a (H⁺/K⁺) ATPase and a herpetoviridae protease for the treatment of a herpetoviridae infection, as required by the method of claim 1, without the disclosure of the applicants' application.

The Office, however, asserts that it is not relevant that the cited art make no mention of treatment of infection caused by herpetoviridae virus infection because "discovery of a new benefit for an old process does not render the old process patentable" based upon the theory of inherency.¹⁵ To properly support a determination of inherency, it is incumbent on the Examiner to first provide rationale or evidence tending to show inherency.¹⁶ In establishing this rationale or evidence, the Examiner must provide a basis in fact and/or technical reasoning to support the determination that the allegedly inherent characteristic necessarily flows from the teaching of the cited art.¹⁷ Furthermore, the mere fact that a certain characteristic may be present in the prior art is not sufficient to establish the inherency of that characteristic.¹⁸ Only after this initial burden of proof has been met by the Office, does the burden shift to the Applicant.

Against the backdrop of this legal standard, the Office has not properly supported its determination of inherency. Applicant's have not simply discovered a new property inherent to a process disclosed in the cited art. Both Ruwart and Senn-Bilfinger disclose methods to treat either gastrointestinal inflammatory diseases, or diseases resulting from gastric acid secretions. Claim 1 is directed toward a method to treat **herpetoviridae infection** by administering a compound that is a dual inhibitor of a (H⁺/K⁺) ATPase and a herpetoviridae protease. Nowhere does the cited art, alone or taken together, disclose or suggest a method to treat herpetoviridae infection in a subject by administering a compound that is a dual inhibitor of a (H⁺/K⁺) ATPase and a herpetoviridae protease. Lindberg et al. disclose that omeprazole is a (H⁺/K⁺) ATPase inhibitor. But as detailed in applicant's specification, omeprazole **does not** inhibit the viral protease assemblin. As stated by the Office, the compounds disclosed by Ruwart and Senn-Bilfinger are "structurally similar" to omeprazole and would be expected to

¹⁵See Paper 6 at page 4.

¹⁶See MPEP § 2112.

¹⁷Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

¹⁸9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

have the same activity absent evidence to the contrary.¹⁹ Following the Office's logic, the compounds disclosed by Ruwart and Senn-Bilfinger may inhibit a (H⁺/K⁺) ATPase, but would not inhibit a viral protease, as required by the method of claim 1.

Unable to establish a *prima facie* case of obviousness, it appears that the Office has effectively slipped into an improper "obvious to try" analysis, informed by hindsight which Applicants' disclosure affords. But the courts have consistently held that the test for a *prima facie* case of obviousness is not whether an invention is obvious to try.²⁰ Instead, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references, and there must be some reasonable expectation of success. For all the reasons detailed above, the Office has not met this legal standard.

For the foregoing reasons, the Office has failed to establish that claim 1 is *prima facie* obvious in view of Senn-Bilfinger, Ruwart, and Lindberg et al. Moreover, claims 2, 22, 25, and new claim 31 and 32, which depend from claim 1, are likewise patent able over these references for the reasons stated with respect to claim 1 and by reason of the additional requirements that they introduce.

II. Conclusion

In light of the foregoing, Applicants request withdrawal of the final rejection, entry of the claim amendments, withdrawal of the claim rejections, and solicit an allowance of the claims. The Examiner is invited to contact the undersigned attorney should any issues remain unresolved.

If there are any additional charges in this matter, please charge Deposit Account No. 19-1345.

Respectfully submitted,



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¹⁹See Paper 6 at page 4.

²⁰ See In re O'Farrell, 7 U.S.P.Q.2d 1673, 1680-81 (Fed. Cir. 1988).